

CLAIMS

1. An isolated nucleic acid encoding a functional MC4R, or the complement thereof, said nucleic acid comprising a nucleotide sequence selected from the group  
5 consisting of:

(a) a nucleotide sequence which hybridizes under conditions of moderate stringency to the coding region of SEQ ID NO:1;

(b) a nucleotide sequence which hybridizes under conditions of moderate stringency to a polynucleotide which is complementary to the coding region of SEQ  
10 ID NO:1;

(c) a nucleotide sequence which hybridizes under conditions of moderate stringency to the coding region of the feline MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1762**; and

(d) a nucleotide sequence which hybridizes under conditions of  
15 moderate stringency to a polynucleotide which is complementary to the coding region of the feline MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1762**,  
with the proviso that said functional MC4R is not human, porcine, murine, rat or chicken.

2. An isolated nucleic acid encoding a functional MC4R, or the complement thereof, said nucleic acid comprising a nucleotide sequence selected from the group  
20 consisting of:

(a) a nucleotide sequence which hybridizes under conditions of high stringency to the coding region of SEQ ID NO:1;

(b) a nucleotide sequence which hybridizes under conditions of high  
25 stringency to a polynucleotide which is complementary to the coding region of SEQ ID NO:1;

(c) a nucleotide sequence which hybridizes under conditions of high stringency to the coding region of the feline MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1762**; and

(d) a nucleotide sequence which hybridizes under conditions of high  
30 stringency to a polynucleotide which is complementary to the coding region of the feline MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1762**.

3. An isolated nucleic acid comprising a nucleotide sequence that:

(a) encodes a polypeptide according to SEQ ID NO:3; or

(b) encodes a polypeptide encoded by the feline MC4R clone as  
35 deposited with the ATCC and having ATCC Accession No. **PTA-1762**.

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4. The isolated nucleic acid of Claim 3, wherein said nucleic acid has a nucleotide sequence according to SEQ ID NO:1 or the feline MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1762**.

5. An isolated nucleic acid comprising a nucleotide sequence having more than 87.4% identity to SEQ ID NO:1 or the feline MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1762**.

6. An isolated nucleic acid comprising a nucleotide sequence encoding a polypeptide having more than 98.2% identity to SEQ ID NO:3 or the polypeptide encoded by the feline MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1762**.

7. An isolated nucleic acid comprising a nucleotide sequence encoding an ECD of a feline MC4R corresponding to amino acids 1-46, 96-123, 186-190, or 268-279 of SEQ ID NO:3 or of the polypeptide encoded by the feline MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1762**.

8. An isolated nucleic acid comprising a nucleotide sequence encoding a CD of a feline MC4R corresponding to amino acids 70-76, 146-165, 212-244, or 302-333 of SEQ ID NO:3 or of the polypeptide encoded by the feline MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1762**.

9. An isolated nucleic acid encoding a functional MC4R, or the complement thereof, said nucleic acid comprising a nucleic selected from the group consisting of:

(a) a nucleotide sequence which hybridizes under conditions of moderate stringency to the coding region of SEQ ID NO:2;

(b) a nucleotide sequence which hybridizes under conditions of moderate stringency to a polynucleotide which is complementary to the coding region of SEQ ID NO:2;

(c) a nucleotide sequence which hybridizes under conditions of moderate stringency to the coding region of the canine MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1761**; and

(d) a nucleotide sequence which hybridizes under conditions of moderate stringency to a polynucleotide which is complementary to the coding region of the canine MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1761**,

with the proviso that said functional MC4R is not human, porcine, murine, rat or chicken.

10. An isolated nucleic acid encoding a functional MC4R, or the complement thereof, said nucleic acid comprising a nucleic selected from the group consisting of:

(a) a nucleotide sequence which hybridizes under conditions of high stringency to the coding region of SEQ ID NO:2;

5 (b) a nucleotide sequence which hybridizes under conditions of high stringency to a polynucleotide which is complementary to the coding region of SEQ ID NO:2;

(c) a nucleotide sequence which hybridizes under conditions of high stringency to the coding region of the canine MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1761**; and

10 (d) a nucleotide sequence which hybridizes under conditions of high stringency to a polynucleotide which is complementary to the coding region of the canine MC4R as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

11. An isolated nucleic acid comprising a nucleotide sequence that:

(a) encodes a polypeptide according to SEQ ID NO:4; or

15 (b) encodes a polypeptide encoded by the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

12. The isolated nucleic acid of Claim 11, wherein said nucleic acid has a nucleotide sequence according to SEQ ID NO:2 or the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

20 13. An isolated nucleic acid comprising a nucleotide sequence having more than 81.3% identity to SEQ ID NO:2 or the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

25 14. An isolated nucleic acid comprising a nucleotide sequence encoding a polypeptide having more than 98.1% identity to SEQ ID NO:4 or to the polypeptide encoded by the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

30 15. An isolated nucleic acid comprising a nucleotide sequence encoding an ECD of a canine MC4R corresponding to amino acids 1-46, 98-124, 187-191, or 268-279 of SEQ ID NO:4 or of the polypeptide encoded by the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

16. An isolated nucleic acid comprising a nucleotide sequence encoding a CD of a canine MC4R corresponding to amino acids 69-77, 147-163, 216-244, or 302-333 of SEQ ID NO:4 or of the polypeptide encoded by the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

18. An expression vector comprising the nucleic acid of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 in operative association with a nucleotide regulatory element that controls expression of the polypeptide encoded by said nucleotide sequence.

20. A genetically engineered host cell comprising the nucleic acid of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 wherein said nucleic acid is in operative association with a nucleotide regulatory element that controls expression of said nucleotide sequence in the host cell.

22. A substantially pure polypeptide comprising the amino acid sequence of :

(d) the canine MC4R clone as deposited with the ATCC and having the ATCC Accession NO. **PTA-1761**;

(f) an ECD of a canine MC4R corresponding to amino acids 1-46, 98-124, 187-191, or 268-279 of SEQ ID NO:4 or of the polypeptide encoded by the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**;

(h) a CD of a canine MC4R corresponding to amino acids 69-77, 147-163, 216-244, or 302-333 of SEQ ID NO:4 or of the polypeptide encoded by the canine MC4R clone as deposited with the ATCC and having ATCC Accession No. **PTA-1761**.

23. An antibody that immunospecifically binds the polypeptide of Claim 21.

24. A method for producing a recombinant polypeptide, comprising:

(a) culturing a host cell transformed with the expression vector of Claim 18 and which expresses the recombinant polypeptide; and

(b) recovering the recombinant polypeptide from the cell culture.

25. A composition comprising the polypeptide of Claim 21 and a carrier.

5 26. A method for detecting a polynucleotide of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 in a sample, comprising:

(a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to form the complex; and

(b) detecting the complex,

10 so that if a complex is detected, a polynucleotide of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 is detected.

27. A method for detecting a polynucleotide of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 in a sample, comprising:

15 (a) contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to a polynucleotide of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 under such conditions; and

b) amplifying the annealed polynucleotides,

so that if a polynucleotide is amplified, the polynucleotide of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 is detected.

20 28. The method of Claim 27, wherein the polynucleotide is an RNA molecule that encodes a functional MC4R, and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide.

29. A method for identifying a compound that binds to the polypeptide of Claim 21, comprising:

25 (a) contacting a compound with the polypeptide of Claim 21 for a time sufficient to form a polypeptide/compound complex; and

b) detecting the complex,

so that if a polypeptide/compound complex is detected, a compound that binds to a polypeptide of Claim 19 is identified.

30 30. A method for identifying a compound that binds to the polypeptide of Claim 21, comprising:

(a) contacting a compound with a polypeptide of Claim 21, in a cell, for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in said cell; and

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so that if a polypeptide/compound complex is detected, a compound

5     ✓     31.     A method of modulating activity of the polypeptide of Claim 21, comprising contacting a cell that expresses the polypeptide with a compound that modulates activity of the polypeptide for a time sufficient to modulate said activity.

(a) contacting a cell line that expresses the polynucleotide of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 with a test compound in the presence of an MC4R agonist; and

in which antagonists are identified as those compounds that inhibit  
15 both the binding and cellular effects of the MC4R agonist on the cell line.

(a) contacting a cell line that expresses the polynucleotide of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 with a test compound in the presence and in the absence of an MC4R agonist;

(c) determining whether, in the absence of the MC4R agonist, the test compound mimics the cellular effects of the MC4R agonist on the cell line,

in which agonists are identified as those test compounds that inhibit  
25 the binding but mimic the cellular effects of the MC4R agonist on the cell line.

35. A method for screening and identifying antagonists of MC4R comprising:

(a) contacting the polypeptide of Claim 21 with a random peptide library

30 such that the polypeptide will recognize and bind to one or more peptide species within the library;

(d) determining whether the test compound inhibits the binding and

cellular effects of an MC4R agonist,

in which antagonists are identified as those peptides that inhibit both the binding and cellular effects of the MC4R agonist.

36. A method for screening and identifying agonists of MC4R comprising:

(a) contacting the polypeptide of Claim 21 with a random peptide library  
5 such that the polypeptide will recognize and bind to one or more peptide species within the library;

(b) isolating a polypeptide/peptide combination;

(c) determining the sequence of the peptide isolated in step (b); and

(d) determining whether, in the absence of a MC4R agonist, the peptide  
10 mimics the cellular effects of the MC4R agonist,

in which agonists are identified as those peptides that inhibit the binding of the MC4R agonist to a MC4R polypeptide but mimic the cellular effects of the MC4R agonist.

37. A method of modulating activity of the polypeptide of Claim 21, comprising  
15 contacting the polypeptide with a compound that modulates activity of the polypeptide for a time sufficient to modulate said activity.

38. A method of modulating the endogenous enzymatic activity of MC4R in an animal comprising administering to the animal an amount of an MC4R ligand effective to modulate said endogenous enzymatic activity.

39. The method of Claim 38, wherein the animal is a cow, a pig, a goat, a sheep, a horse, a dog, or a cat.

40. The method of Claim 38 in which the ligand to said MC4R receptor is an MC4R agonist.

41. The method of Claim 38 in which the ligand to said MC4R receptor is an  
25 MC4R antagonist.

42. The antagonist of Claim 41 that is a monoclonal antibody that immunospecifically binds to an epitope of said MC4R.

43. The method of Claim 38 in which the enzymatic activity of said MC4R is increased.

44. The method of Claim 38 in which the enzymatic activity of said MC4R is  
30 decreased.

45. A transgenic animal in which the nucleic acid of Claim 1 or 9 is an expressed transgene contained in the genome of the animal.

46. A transgenic animal in which expression of genomic sequences encoding the  
35 polypeptide of Claim 21 is prevented or repressed.

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67. The method of Claim 47 wherein the ligand is part of a pharmaceutical  
35 composition.



68. The method of Claim 67 wherein the preparation is administered orally, transdermally, or by slow release subcutaneous implants/pellets.

69. A kit comprising a pharmaceutical composition comprising an MC4R ligand.

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Pub. No. 7,199,999